# FDA Perspective on Assessment of Drugs – Abuse Potential & Abuse Deterrence

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# Outline

- Context:  FDA Efforts to Address Prescription Opioids Abuse
- Improving the Science of Abuse Assessment
- Supporting the Development of Abuse-Deterrent Formulations of Opioids
  - Policy Framework and Goals
  - Draft Guidances
  - Remaining Scientific, Policy and Process Issues

# Overall Message

- Incentivizing abuse-deterrent formulations of opioids is one important part of ongoing FDA work to improve the assessment of drugs for their abuse potential
- The work on abuse-deterrent formulations of opioids is taking place within a larger policy framework aimed at addressing opioid abuse
- Assessment of abuse potential, either for new drugs, or for abuse-deterrent formulations of opioids, must be based on rigorous science

# FDA Confronting Prescription Drug Abuse and Misuse

- Improving the use of opioids through careful and appropriate science and regulations
- Improving the use of opioids through education of prescribers and patients
- Improving the safe use of opioids through partnership and collaboration
- Improving the use of opioids through improved science

# Drugs



**Drug Safety and Availability**
Information by Drug Class

## Resources for You

- Opioid Medications
- Timeline of Key Opioid Actions
- Questions and Answers: REMS for Extended-Release and Long-Acting Opioids
- FDA Encourages Prescribers to Seek Training to Safely Prescribe Opioids

## Attention Prescribers: FDA seeks your help in curtailing the U.S. opioid epidemic

FDA is asking all prescribers of opioids to ensure they have thorough knowledge of the FDA-approved product labeling for the opioids they prescribe, and to ensure they have adequate training in opioid therapy. Below is our Open Letter to prescribers. We encourage all prescribers to help curb our nation's opioid epidemic!

**View and print full article - Attention Prescribers: Curtailing Opioid Epidemic [PDF - 137KB]**

Summary & Introduction | Take Training | Know Opioid Labels | *Key Label Examples* | Educate Patients | Conclusion

### Summary

- In light of the expanding opioid epidemic in the U.S., FDA urges prescribers to take advantage of training on opioid prescribing, available as of March 1, 2013. This voluntary training will be provided at little to no cost through accredited continuing education activities supported by independent education grants.
- Taking advantage of training opportunities on opioid therapy, now and in the future, is one of three key roles that FDA sees for prescribers in helping to curtail this pervasive problem. The other two are: knowing the content of the most current drug labels for the opioids they prescribe, and educating patients about the appropriate use of opioids, their potential risks, and proper disposal techniques.
- FDA-approved drug labels are frequently updated based on additional science, new benefit-risk information, or public health implications regarding the medication. Labels of extended release and long-acting opioid drugs were changed in July, 2012.

### Introduction

Misuse and abuse of prescription opioids has reached epidemic proportions in the U.S. While much of the problem is attributable to illicit use, appropriate use of medications for pain may also lead to unnecessary adverse events, addiction, and death for some patients. *No group can be more effective in reducing this trend than our nation's front-line health care professionals, especially physicians and other prescribers.*

# Improving the Science of Abuse Assessment

# Goals of FDA Efforts to Improve Abuse Assessment

- Improving the science of abuse assessment before a drug is on the market, so that appropriate controls are put in place to reduce the likelihood that a drug will be abused after marketing
- Protecting public health through accurate labeling of drugs that can be abused

# Improving the Science of Abuse Assessment

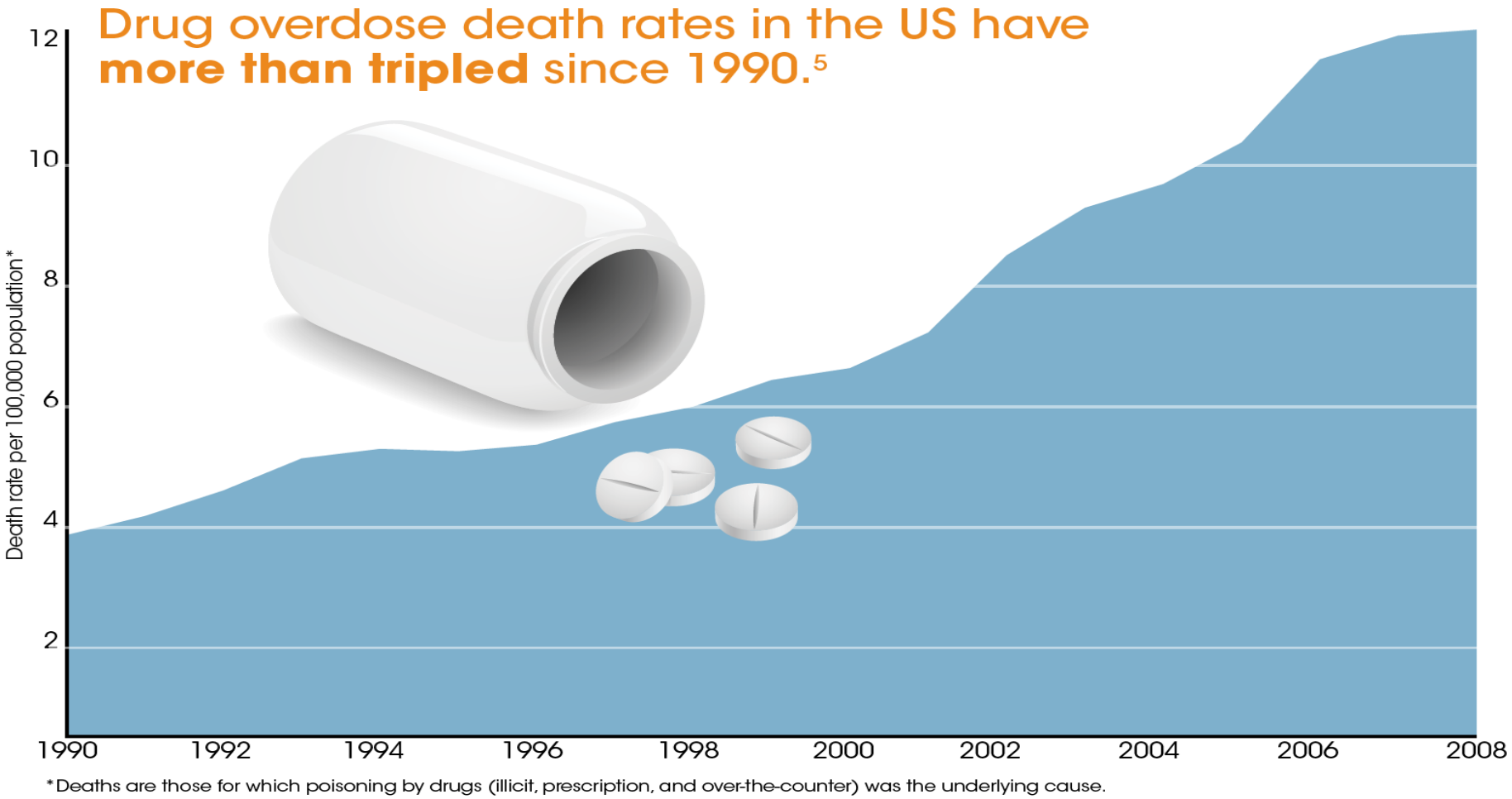
- Draft Guidance: Assessment of Abuse Potential of Drugs, issued January 2010
  - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM198650.pdf
  - Discusses use of safety information from all areas of the NDA to predict abuse potential of new drugs, including brief discussion of abuse deterrence formulations

# Next Steps

- Finalizing draft Guidance informed by:
  - Follow-up meeting to discuss draft Guidance November 10, 2011
  - Comments to Docket
  - Experience in abuse liability assessment, including assessment of abuse-deterrent formulations of opioids
- Areas of focus:
  - Advice on sequential testing for abuse potential
  - Advice on conduct of Human Abuse Potential study
  - Need to integrate abuse assessment into overall 21st Century Review process as a part of drug development

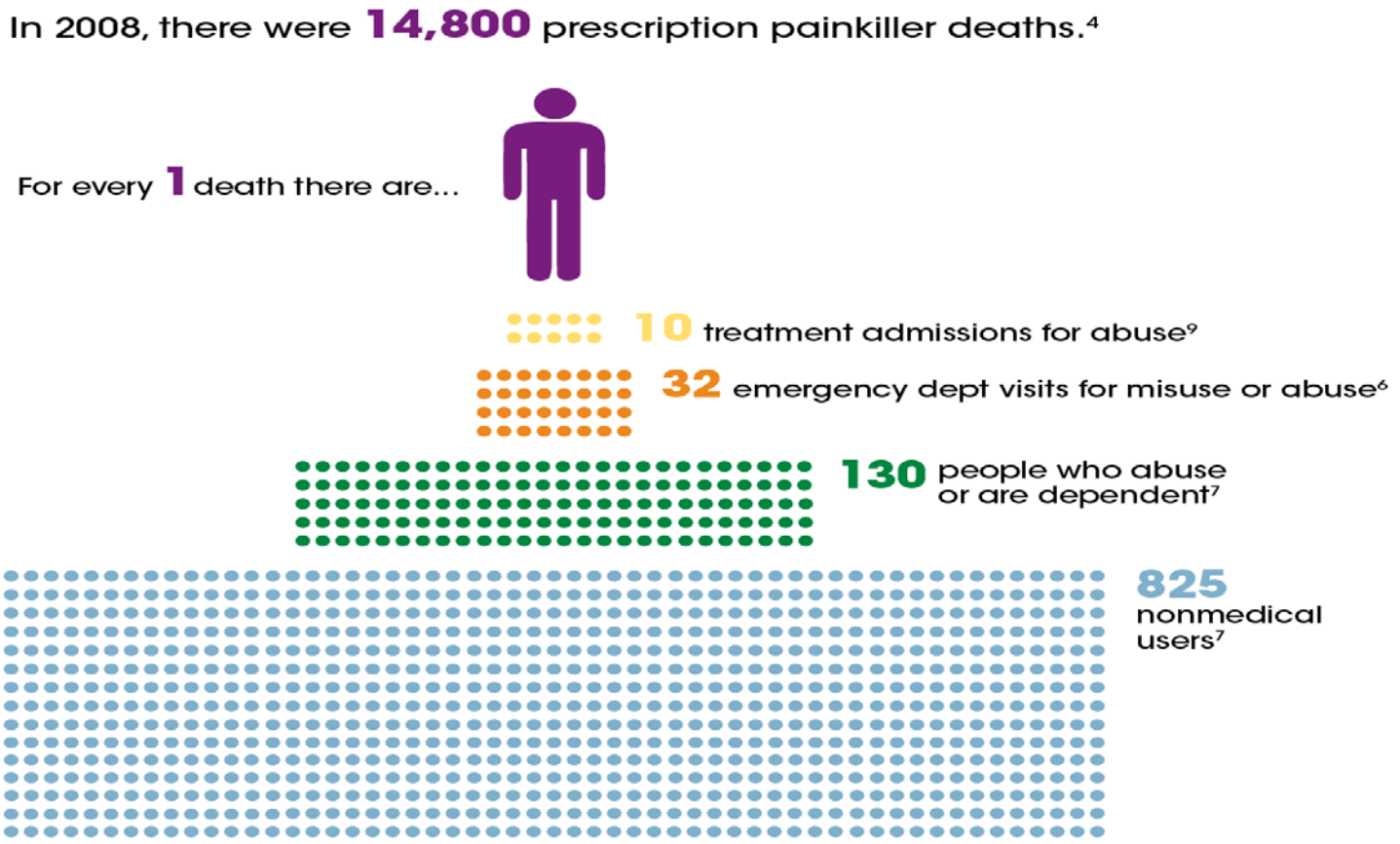
# Improving the Development and Use of Abuse-Deterrent Formulations of Opioids

# A Major Public Health Issue




Source: CDC NCIPC November 2011

# Opioid Deaths Are the "Tip of the Iceberg"




Source: CDC NCIPC November 2011

# FDA Public Health Goals

- Provide appropriate access to pain treatments for patients, including opioids drugs
- Reduce the misuse and abuse of prescription opioids

# Developing Guidance on Abuse-Deterrent Formulations

- Advisory Committees
  - Topic at several meetings: 2008 to 2014
  - Tone generally conservative about data needed to conclude a new formulation is abuse-deterrent
- Public/Congressional interest in issue pronounced….

# Innovator Abuse-Deterrent Opioids Guidance

- Promised as part of Office of National Control Policy (ONDCP) Rx Drug Abuse Plan (2011)
- Mandated under FDASIA
  - Goal date for Draft January 9, 2013 (met)
  - Goal date for Final June, 2015 (met)

# Other FDA Work to Support AD Formulation Development

- Scientific Research
- Regulatory Activities
  - Decisions on applications
  - Sponsor discussions as a part of development
- Public Discussion and Comment
  - Public meetings, including meeting held October 30, 31, 2014
  - Comments on draft Guidance
  - Citizen Petitions

# Twin Goals for Abuse Deterrent (AD) Formulations of Opioids

- Incentivize the development of opioid medications with progressively better abuse-deterrent properties and support their widespread use
- Assure appropriate development and availability of generics, reflecting their importance in US healthcare

# FDA Policy Framework for the Overall Assessment and Regulation of AD Opioids

- **Goal: support the development and use of progressively-better AD opioids:**
  - Giving a labeling claim for specific product
  - Also blocking the approval of other drugs that lack the same (or better) abuse-deterrent properties
  - Also, taking action against existing products with the same opioid
  - Also, taking action against existing products, including those with different opioids

# Three Stages in Development of AD Opioids

- **Early**: market has a small number of AD products using early AD technology
  - Case by case decision-making
- **Intermediate**: multiple products approved as abuse deterrent using various technologies
  - Fuller set of regulatory issue identified,
  - Guidance outlining FDA's approach for brand name and generic development is refined
  - Actions potentially shift to class-wide scope
- **Late**: AD formulations of all major opioids marketed
  - Focus is on supporting iterative improvement in AD technologies

# Essential Features of Successful AD Formulations

- The product must deliver a consistent and effective dose of opioid when used as labeled by pain patients
- The product's potentially abuse-deterrent properties can be expected to, or actually do, result in a significant reduction in that product's abuse potential
  - Labeling must be based on scientific data
  - Labeling based on pre-market studies needs confirmed using post-market data

# Regulatory Activity Related to AD Opioids

- 4 products given abuse-deterrent claims in label
  - OxyContin (oxycodone, crush/extraction resistant)
  - Embeda (morphine/naltrexone, naltrexone is aversive/precipitates withdrawal when abused)
  - Targeniq (oxycodone hydrochloride and naloxone, naloxone aversive)
  - Hysingla (hydrocodone, crush/extraction resistant)
- >30 active INDs being discussed with CDER
  - New technologies being explored

# Ongoing Work: Generics Abuse-Deterrent Opioids Guidance

- Generic products represent a significant fraction of all prescriptions in the US today
- No current guidance for ANDA sponsors or reviewers
- A generic opioid product should be no less abuse-deterrent than its RLD under the manipulation conditions and routes of abuse that are practiced by drug abusers
  - This will ensure abusers do not seek out generics as easier to abuse

# Next Steps

- Implementation of AD Guidance
- Releasing draft Generics AD Guidance to support generics development for comment
- Finalization of the Guidance on the Assessment of Abuse Potential
  - Informed by the work on the abuse deterrent formulations guidance

# Current Challenges in Abuse Liability Assessment: Science

- Real-world data are needed to assess whether the approval of an AD opioid product actually reduces opioid-related abuse, misuse, addiction, overdose, or death
  - Post-marketing Requirements for additional studies for all drugs with approved abuse-deterrent language
- Additional work needed:
  - Use of non-clinical models and data
  - Adverse Event collection and assessment

# Current Challenges in Abuse Liability Assessment: Process

- Incorporating abuse liability assessment into drug development efficiently:
  - Timely interactions with sponsors to design and conduct studies and discuss results where needed
  - High-quality, complete submissions by sponsors

# Current Challenges in Abuse Liability Assessment and AD Formulations: Policy

- Incentivizing innovation:
  - Primary incentive FDA has available is labeling
  - Challenge to encourage iterative development of abuse-deterrent formulations
  - Challenge to encourage uptake of these products by payers
- Managing expectations: abuse-deterrent opioids will not ‘prevent’ abuse, and are not ‘silver bullets’

# Summary

- FDA is working across many areas to
  - Improve the assessment of abuse, including for abuse-deterrent formulations of opioids
  - Encourage the development of new products to treat pain that will offer improved safety and efficacy
- Within this broadened range of activities, our regulatory mission remains at the heart of FDA role in opioids
  - FDA will act within its authorities, based on science, in support of our public health mission